Imnovid® (pomalidomide)

Information for Healthcare Professionals

Brochure

INTRODUCTION

This Brochure contains the information needed for prescribing and dispensing Imnovid® (pomalidomide), including information about the Pregnancy Prevention Programme (PPP). Please also refer to the Summary of Product Characteristics (SmPC) for further information. *http://www.medicinesauthority.gov.mt/home?l=1*

Imnovid in combination with bortezomib and dexamethasone is indicated in the treatment of adult patients with multiple myeloma who have received at least one prior treatment regimen including lenalidomide.

The recommended starting dose of Imnovid (pomalidomide) is 4 mg orally once daily on Days 1 to 14 of repeated 21-day cycles. Pomalidomide is administered in combination with bortezomib and dexamethasone. The recommended starting dose of bortezomib is 1.3 mg/m^2 intravenous or subcutaneous once daily, on the days shown in Table 1 in Section 4.2 of the SmPC. The recommended dose of dexamethasone is 20 mg orally once daily, on the days shown in Table 1 in Section 4.2 of the SmPC. Treatment with pomalidomide combined with bortezomib and dexamethasone should be given until disease progression or until unacceptable toxicity occurs.

For patients >75 years of age, the starting dose of dexamethasone is 10 mg once daily on Days 1, 2, 4, 5, 8, 9, 11 and 12 of each 21day cycle for Cycles 1 to 8 and 10 mg once daily on Days 1, 2, 8 and 9 of each 21-day cycle for Cycles 9 and onwards. No dose adjustment is required for pomalidomide. For bortezomib, refer to the current SmPC for additional information.

Imnovid in combination with dexamethasone is indicated in the treatment of adult patients with relapsed and refractory multiple myeloma (MM) who have received at least two prior treatment regimens, including both lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy.

The recommended starting dose of Imnovid (pomalidomide) is 4 mg orally once daily on Days 1 to 21 of repeated 28-day cycles (21/28 days). The recommended dose of dexamethasone is 40 mg orally once daily on Days 1, 8, 15 and 22 of each 28-day treatment cycle. Treatment with pomalidomide combined with dexamethasone should be given until disease progression or until unacceptable toxicity occurs.

For patients >75 years of age, the starting dose of dexamethasone is 20 mg once daily on Days 1, 8, 15 and 22 of each 28-day treatment cycle. No dose adjustment is required for pomalidomide.

The following section contains advice to Healthcare Professionals about how to minimise the main risks associated with the use of pomalidomide. Please refer also to SmPC (Sections 4.2 Posology and method of administration, 4.3 Contraindications, 4.4 Special warnings and precautions for use and 4.8 Undesirable effects).

In general, most adverse reactions occurred more frequently during the first 2 to 3 months of treatment. Please note that the posology, adverse event profile and recommendations outlined herein, particularly in respect thrombocytopenia, relate to the use of pomalidomide within its licensed indication. There is currently insufficient evidence regarding safety and efficacy in any other indication.

RISKS OF POMALIDOMIDE

Thrombocytopenia

Thrombocytopenia is one of the major dose-limiting toxicities of treatment with pomalidomide.

It is therefore encouraged to monitor complete blood counts - including platelet count - weekly for the first 8 weeks and monthly thereafter.

A dose modification or interruption may be required. Patients may require use of blood product support and /or growth factors.

Thrombocytopenia can be managed with dose modifications and/or interruptions.

Recommended dose modifications during treatment and restart of treatment with Imnovid® are outlined in the table below:

Dose modification or interruption instructions

Toxicity	Dose Modification
Thrombocytopenia	
• Platelet Count <25 x 10^9/l	Interrupt pomalidomide treatment, follow CBC weekly.
• Platelet Count return to ≥50 x 10^9/l	Resume pomalidomide treatment at one dose lower than previous dose.
For each subsequent drop <25 x 10^9/l	Interrupt pomalidomide treatment.
Platelet count return to ≥50 x 10^9/l	Resume pomalidomide treatment at one dose level lower than the previous dose.

CBC – Complete Blood Count

To initiate a new cycle of pomalidomide, the platelet count must be ≥50 x 10^9/l.

For other Grade 3 or 4 adverse reactions judged to be related to pomalidomide, stop treatment and restart treatment at 1 mg less than the previous dose when an adverse reaction has resolved to ≤ Grade 2 at the physician's discretion. If adverse reactions occur after dose reductions to 1 mg, then the medicinal product should be discontinued (see Section 4.2 of the SmPC).

Thrombocytopenia occurred in 27.0% of patients who received POM + LD-Dex, and 26.8% of patients who received HD-Dex. Thrombocytopenia was Grade 3 or 4 in 20.7% of patients who received POM + LD-Dex and in 24.2% who received HD-Dex. In POM + LD-Dex treated patients, thrombocytopenia was infrequently serious in 1.7% of patients, led to dose reduction in 6.3% of patients, to dose interruption in 8% of patients and to treatment discontinuation in 0.7% of patients (see Section 4.8 of the SmPC).

Cardiac failure

Cardiac events, including congestive cardiac failure, pulmonary oedema and atrial fibrillation (see Section 4.8 of the SmPC), have been reported, mainly in patients with pre-existing cardiac disease or cardiac risk factors. Appropriate caution should be exercised when considering the treatment of such patients with pomalidomide, including periodic monitoring for signs or symptoms of cardiac events (see Section 4.4 of the SmPC).

PREGNANCY PREVENTION PROGRAMME

- Pomalidomide is structurally related to thalidomide, a known human teratogenic substance that causes severe life-threatening birth defects. Pomalidomide induced, in rats and rabbits, malformations similar to those described with thalidomide.
- If pomalidomide is taken during pregnancy, a teratogenic effect in humans is expected. Pomalidomide is therefore contraindicated in pregnancy and in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme described in this pack are met.
- It is a requirement of the Pregnancy Prevention Programme that all Healthcare Professionals ensure that they have read and understood this brochure before prescribing or dispensing pomalidomide for any patient.
- All men and all women of childbearing potential should undergo, at treatment initiation, counselling of the need to avoid pregnancy
- Patients should be capable of complying with the requirements of safe use and handling of pomalidomide.
- Patients must be provided with the appropriate educational Patient Brochure and Patient Card and/or equivalent tool.
- For WCBP the patient card has to be filled in with every prescription and presented to the Pharmacy with updated pregnancy testing filled in. For WNCBP and Males, the patient card is filled on initiation of treatment and kept in the patient's file.
- The description of the Pregnancy Prevention Programme and the categorisation of patients based on sex and childbearing potential is set out in the attached Algorithm.

PRESCRIBING POMALIDOMIDE

Women of Childbearing Potential:

- Prescriptions of pomalidomide should be limited to a maximum duration of 4 consecutive weeks of treatment according to the approved indications dosing regimens (posology; see Introduction) and continuation of treatment requires a new prescription.
- Do not dispense to a woman of childbearing potential unless the pregnancy test is negative and was performed within 3 days prior to the prescription.

All Other Patients:

- For all other patients, prescriptions of pomalidomide should be limited to a maximum duration of 12 consecutive weeks and continuation of treatment requires a new prescription.

Female Patients:

Determine if a woman is not of childbearing potential.

- The following are considered to not have childbearing potential.
  - Age ≥ 50 years and naturally amenorrhoeic for ≥ 1 year*
  - Confirmed premature ovarian failure if confirmed by specialist gynaecologist
  - Previous bilateral salpingo-oophorectomy, or hysterectomy
  - XY genotype, Turner syndrome, uterine agenesis.

*Amenorrhoea following cancer therapy or during breastfeeding does not rule out childbearing potential.

You are advised to refer your patient for a gynaecological opinion if you are unsure whether or not she meets these criteria.

PPP Advice for Women of Childbearing Potential

Women of childbearing potential must never take pomalidomide if:

- Pregnant
- Breastfeeding
- A woman who is able to become pregnant, even if not planning to become pregnant, unless all of the conditions of the Pregnancy Prevention Programme are met.

In view of the expected teratogenic risk of pomalidomide, foetal exposure should be avoided.

- Women of childbearing potential (even if they have amenorrhoea) must:
  - use at least one effective method of contraception for at least 4 weeks before therapy, during therapy, and until at least 4 weeks after pomalidomide therapy finished, and even in case of dose interruption or
  - commit to absolute and continuous abstinence confirmed on a monthly basis

  AND

  - have a medically supervised negative pregnancy test prior to issuing a prescription (with a minimum sensitivity of 25 mIU/ml) once she has been established on contraception for at least 4 weeks, at least every 4 weeks during therapy (this includes dose interruptions) and at least 4 weeks after the end of therapy (unless confirmed tubal sterilisation). This includes those women of childbearing potential who confirm absolute and continued abstinence. *Add here available tests according to local practice.*

- Patients should be advised to inform the physician prescribing her contraception about the pomalidomide treatment.
- Patients should be advised to inform you if a change or stop of method of contraception is needed.

If not established on effective contraception, the patient must be referred to an appropriately trained health care professional for contraceptive advice in order that contraception can be initiated.

The following can be considered to be examples of suitable methods of contraception:

- Implant
- Levonorgestrel-releasing intrauterine system (IUS)
- Medroxyprogesterone acetate depot
- Tubal sterilisation
- Sexual intercourse with a vasectomised male partner only; vasectomy must be confirmed by two negative semen analyses
- Ovulation inhibitory progesterone-only pills (i.e. desogestrel)

Because of the increased risk of venous thromboembolism in patients with multiple myeloma taking pomalidomide and dexamethasone, combined oral contraceptive pills are not recommended. If a patient is currently using combined oral contraception the patient should switch to one of the effective methods listed above. The risk of venous thromboembolism continues for 4 to 6 weeks after discontinuing combined oral contraception. The efficacy of contraceptive steroids may be reduced during co-treatment with dexamethasone.

Implants and levonorgestrel-releasing intrauterine systems are associated with an increased risk of infection at the time of insertion and irregular vaginal bleeding. Prophylactic antibiotics should be considered particularly in patients with neutropenia.

Insertion of copper-releasing intrauterine devices is not recommended due to the potential risks of infection at the time of insertion and menstrual blood loss which may compromise patients with severe neutropenia or severe thrombocytopenia.

Your patient should be advised that if a pregnancy does occur whilst she is receiving pomalidomide, she must stop treatment immediately and inform her physician immediately.

PPP Advice for Men

- In view of the expected teratogenic risk of pomalidomide, foetal exposure should be avoided.
- Inform your patient which are the effective contraceptive methods that his female partner can use.
- Pomalidomide is present in human semen. As a precaution, all male patients taking pomalidomide, including those who have had a vasectomy as seminal fluid may still contain pomalidomide in the absence of spermatozoa, should use condoms throughout treatment duration, during dose interruption and for at least 7 days after cessation of treatment if their partner is pregnant or of childbearing potential and has no contraception.
- Male patients should not donate semen or sperm during treatment, during dose interruptions and for at least 7 days following discontinuation of pomalidomide.
- Patients should be instructed that if their partner becomes pregnant whilst he is taking pomalidomide or within 7 days after he has stopped taking pomalidomide he should inform his prescriber immediately. The partner should inform her physician immediately. It is recommended that she be referred to a physician specialised in teratology for evaluation and advice.

Disposal of unwanted medicine

- Capsules should not be opened or crushed. If powder from pomalidomide makes contact with the skin, the skin should be washed immediately and thoroughly with soap and water. If pomalidomide makes contact with the mucous membranes, they should be thoroughly flushed with water.
- Patients should be advised never to give pomalidomide to another person and to return any unused capsules to their pharmacist at the end of the treatment.

Blood donation

- All patients should not donate blood during treatment (including dose interruptions) and for at least 7 days after cessation of treatment with pomalidomide.

Requirements in the event of a suspected pregnancy

- Stop treatment immediately if female patient.
- Refer female patient to a physician specialised or experienced in teratology for evaluation and advice.
- Notify Celgene of all suspected pregnancies in female patients or partners of male patients.
  - Pregnancy Capture Form is included in this pack
  - Call AM Mangion Ltd on + 356 23976333
  - Celgene will wish to follow-up with you the progress of all suspected pregnancies in female patients or partners of male patient cases.
  - Reporting of pregnancy/suspected pregnancy must be immediate, upon knowledge of the event.

REPORTING OF ADVERSE REACTIONS

The safe use of pomalidomide is of paramount importance. As part of Celgene's ongoing safety monitoring, the company wishes to learn of Adverse Reactions that have occurred during the use of pomalidomide. Adverse Reaction report forms are included in this Healthcare Professional Kit.

Suspected adverse events must be reported to Medicines Authority - http://www.medicinesauthority.gov.mt/adrportal

CONTACT DETAILS

For information and questions on the risk management of Celgene's products, and the Pregnancy Prevention Programme, please contact:

AM Mangion Ltd

Regulatory Office - Mangion Building, New Street off Valletta Road, Luqa- Malta

Tel - + 356 23976333

Email – pv@ammangion.com

Checklist for Counselling

This checklist is to assist you with counselling a patient before they commence Imnovid® (pomalidomide) treatment in order to assure it is used safely and correctly. Please choose the applicable column for the risk category of the patient and refer to the counselling messages provided.

Did you inform your patient:	**Male Patients**	**Women of Non-Childbearing Potential***	**Women of Childbearing Potential**
• Of the expected teratogenic risk to the unborn child?			
• Of the need for effective contraception** for at least 4 weeks before starting treatment, throughout the entire duration of treatment, including during treatment interruptions, and for at least 4 weeks after the end of treatment, or absolute and continued abstinence?	**N/A**	**N/A**	
• That she must comply with advice on contraception even if she has amenorrhoea?	**N/A**	**N/A**	
• Which are the effective contraceptive methods that she or the female partner of a male patient can use?		**N/A**	
• Of the expected consequences of pregnancy and the need to stop treatment and consult rapidly if there is a risk of pregnancy?		**N/A**	
• Of the need to use condoms, including those who have had a vasectomy as seminal fluid may still contain Imnovid® (pomalidomide) in the absence of spermatozoa, throughout treatment duration, during dose interruption, and for at least 7 days after cessation of treatment if partner is pregnant or of childbearing potential not using effective contraception?		**N/A**	**N/A**
• Of the need not to donate semen or sperm during treatment, during dose interruptions, and for at least 7 days following discontinuation?		**N/A**	**N/A**
• Of the hazards and necessary precautions associated with use of pomalidomide?			
• Not to share medication?			
• To return unused capsules to pharmacist?			
• Not to donate blood whilst taking pomalidomide, during treatment interruptions and for at least 7 days following discontinuation?			
• About the thromboembolic risk and the possible requirement to take thromboprophylaxis during treatment with pomalidomide?			

Can you confirm that your patient:	**Male Patients**	**Women of Non-Childbearing Potential**	**Women Childbearing Potential**
• Was referred to a contraceptive consultant, if required?	**N/A**	**N/A**	
• Is capable of complying with contraceptive measures?		**N/A**	
• Agreed to undergo pregnancy testing at least in 4 weekly intervals unless confirmed tubal sterilisation?	**N/A**	**N/A**	
• Had a negative pregnancy test before starting treatment even if absolute and continued abstinence?	**N/A**	**N/A**	•

* Refer to HCP Brochure for criteria to determine if patient is a woman of non-childbearing potential.

** Refer to HCP Brochure for information on contraception.

TREATMENT FOR A WOMAN OF CHILDBEARING POTENTIAL CANNOT START UNTIL PATIENT IS ESTABLISHED ON AT LEAST ONE EFFECTIVE METHOD OF CONTRACEPTION FOR AT LEAST 4 WEEKS PRIOR TO INITIATION OF THERAPY OR COMMITS TO COMPLETE AND CONTINUED ABSTINENCE AND PREGNANCY TEST IS NEGATIVE!

▼ ***This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions via www.medicinesauthority.gov.mt/adrportal***

Description of the Pregnancy Prevention Programme and Patient Categorisation Algorithm